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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,941	09/24/2003	David A. Brake	15471ZYZ (PC9590F)	4787

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Dr. Peter C. Richardson
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

EXAMINER

PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/669,941

Applicant(s)

BRAKE ET AL.

Examiner

Ginny Portner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 24 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-4, 6-9 and 11-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-4, 6-9, 11-20, 22-27 and 29-32 is/are rejected.
- 7) ☐ Claim(s) 21, 24 and 28 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Claims 1-4, 6-9, 11-32 are pending.

Information Disclosure Statement

1. The information disclosure statement filed September 24, 2003 has been considered.

Allowable Subject Matter

2. Claims 21 and 28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Objections

3. Claim 24 is objected to because of the following informalities: Claim 24 recites the positive active voice methods step of “administering” and also recite the conditional phrase “when administered as a live vaccine, and a veterinary acceptable carrier”; the tenses for the term administer are not in agreement and the immune response that protects is only provided when the live vaccine is administered with a “veterinary acceptable carrier”. The method is a method of vaccinating, but only cells are provided in the “administering” step and the “veterinary acceptable carrier” would also be required to accomplish the recited intended use of the claimed method. Amendment of the claim to recite positive characteristics and the combination of components which would accomplish the recited intended use of the preamble could obviate this objection. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 2,7,18, 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 7, 18, 25 recite the relative phrase “temperature sensitive”; this phrase does not define how these strains differ from the strains of the independent claims from which they depend. All proteins are temperature sensitive to some extent, some more than others, and strains of *Neospora* which comprise proteins are also considered to be temperature sensitive. How do the strains of claims 2, 7, 18 and 25 structurally differ from the strains of the independent claim? Claims 2, 7, 18 and 25 are descriptive and not further limiting of the independent claim from which they depend as the recitation of a functional characteristic does not distinctly point the structural differences between the claimed inventions. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

6. Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 recites various components for “A combination vaccine”. The claim contains “;”s on lines 6 and 8. It is not clear what is intended to be the invention in view of the claim being set forth in this manner. The clause between the “;”s states “one or more other antigens that trigger an immune response that protects the mammal against a disease or a pathological condition”. It is not clear whether ^{the} phrase ^{is} defining a non-specific antigenic adjuvant, an

additional strain of cells, or additional vaccine antigens for a different pathogen. It appears that a transitional phrase is missing. Clarification of this phrase is requested.

Claim Rejections - 35 U.S.C. § 112

7. Claims 1-4, 6-9, 11-12, 13-20, 22-27, 29-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions that induce an immune response against Neospora and other additional immunogens, does not reasonably provide enablement for the use of the compositions that will induce a protective immune response based upon any type of attenuation or modification, nor enabling for the treatment of pre-existing infection by Neospora or prevent Neospora prior to infection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification and the claims are directed to methods of preparing of compositions(vaccines) that will trigger a protective immune response in a mammal. The utilization of any attenuated strain would not predictably induce a protective immune response. Andrianarivo et al (International Journal of Parasitology) is cited to show a commercially available vaccine composition of Neospora caninum which failed to induce a protective immune response upon challenge with the homologous pathogen.

The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity infection or disease induction. The specification does not provide substantive evidence that the claimed vaccines are capable of inducing protective immunity utilizing any strain of Neospora that is attenuated relative to the parent strain. This demonstration is required

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for the skilled artisan to be able to use the claimed vaccines for their intended purpose of preventing infections caused by *Neospora* and additional antigens.

Utilization of any attenuated strain would not predictably induce a protective immune response. Support for unpredictability of strains of *Neospora* to induce a protective immune response is provided through citing

Andrianarivo et al (International Journal of Parasitology) who shows a commercially available vaccine composition of *Neospora caninum* failed to induce a protective immune response upon challenge with the homologous pathogen, and a live composition of culture derived, live, *Neospora caninum* grown in monkey kidney cells that were also not protective against infection (see page 986, col. 1, second paragraph, second half of paragraph; see page 987, col. 1, 4 lines from bottom; page 988, Figure 2 narrative) culture derived *N.caninum* tachyzoites, cultured and administered at week 8.

Anderson et al (2000, abstract) teaches that there “are no proven control methods for the prevention or treatment of neosporosis” (second to last sentence of abstract)..

Innes et al (2002) teach that vaccination has challenges for pregnant mammals, and is questionably feasible to control disease in this population of mammals (see abstract).

Nishikawa et al (2001) teach that a mammal that had previously been infected with *Neospora caninum* became reinfected with chronic infection and teaches the essential component of induction of sufficient levels of interferon-gamma in the early stages of infection to prevent chronic disease Nishikawa et al (2001, abstract) teach that a mammal that had previously been infected with *Neospora caninum* became reinfected with chronic infection and teaches the

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essential component of induction of sufficient levels of interferon-gamma in the early stages of infection to prevent chronic disease.

Compositions which have not been shown to prevent or to treat disease would not be predictable as vaccines; the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced.

Further, the specification fails to provide an adequate enabling written description as to which and what mutations and attenuations would result in a vaccine strain of Neospora. The skilled artisan would be required to de novo locate, identify and characterize the claimed attenuated strains that would function as a vaccine in any animal. The art indicates that it would require undue experimentation to formulate and use a successful vaccine without the prior demonstration of vaccine efficacy.

Claim Rejections - 35 U.S.C. § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

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9. Claims 1-2, 6-7, 11-12, 24-25, 30-31 and 32 are rejected under 35 U.S.C. 102(e) as being anticipated by Conrad et al (US Pat. 5,707,617).

(Instant claims 1-2, 6-7) Conrad et al disclose the instantly claimed invention directed to an culture of cells derived from a pathogenic strain of Neospora (see col. 11, line 45), wherein the (col. 4, line 42) composition of attenuated Neospora (see col. 2, lines 43-51; col. 11, line 35) was able to trigger a protective immune response (see col. 11, lines 46-47). The composition disclosed are combined with a pharmaceutically acceptable carrier (see Conrad et al, col. 2, line 16; col. 11, line 51-65); or

(Instant claim 11, 32) an adjuvant which includes an additional antigen associated with an additional pathogen: Bordetella pertussis, bacterial endotoxin or lipid (see Conrad et al, col. 11, lines 57-58; The combination composition would result in a combination vaccine of live Neospora cells with additional antigens that would trigger an immune response to the additional one or more antigens included in the combination vaccine.), or

(Instant claim 12) the adjuvant is an oil-in-water adjuvant (see Conrad et al, col. 11, line 56).

(Instant claim 24, 25, 29-31) Additionally, Conrad et al discloses a method of vaccinating a mammal against neosporosis, the method comprising the step of:

administering (col. 11, lines 44-47; col. 12, line 3) to the mammal (cow, sheep goats, mice (see col. 12, line 4; col. 8, lines 11-12) an immunologically effective amount (see col. 12, lines 7-8) of a vaccine comprising live cells of a strain derived from a pathogenic parent strain of Neospora (see col. 4, lines 47-50; col. 5, lines 1-11) together with a carrier, adjuvant, or water in oil emulsion (see col. 11, lines 45-67).

Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for

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the prior art's functioning, does not render the old composition patentably new to the discoverer. "The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art".

10. Claims 1-4, 6-9, 13-16, 17-20 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Lindsay et al (Sept. 1995).

(Instant claims 1-4, 6-9) Lindsay et al disclose the instantly claimed invention directed to a composition of cultured *N.caninum* cells that were derived from parent strains of *Neospora caninum* and were designated NC-1, NC-2 and NC-3 (see page 1179, col. 2, Discussion section, paragraph 3). The cultures of cells were used to formulate a sterile composition of cells adjusted to 10^7 in 3 ml of pharmaceutical carrier (see page 1177, sterile HBSS, col. 1, paragraph 5, first sentence).

The strains were attenuated through sub-culturing of the strains which were "maintained by subinoculation into noninfected monolayers every 3 to 4 days" (see page 1177, col. 1, paragraph 5). The sub cultured cells would be sensitive to freezing temperatures and would also be attenuated through one or more passages in in-vitro culture (definition provided in Applicant's specification at page 5, lines 17-27.)

(Instant claim 32) An additional embodiment disclosed in Lindsay was a combination composition that comprises first, second and third antigenic strains of *N caninum* cells, specifically. The combination composition would comprise one or more other antigens that trigger an immune response.

(Instant claims 13-16 and 17-20) The composition was cultured (modifying), selected, formulated (prepared) into compositions and administered to a mammal as an inoculums and

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administered intramuscularly or intravenously. The cultured cell compositions and method of preparing and immunizing of Lindsey inherently anticipate the now claimed compositions.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594

11. Claims 1-3, 13-15, 17-19 are rejected under 35 U.S.C. 102(a) as being anticipated by Lindsay et al (January 1996, abstract, different inventive entity).

Lindsay et al disclose the production of mutated strains of *Neospora caninum* through treatment with N-methyl-N-nitrosoguanidine, wherein the mutated strains would be attenuated and temperature sensitive, at least to freezing temperatures. Inherently the cultured *N.caninum* cells of Lindsay et al anticipate the now claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594

12. Claims 1-4 and 6-9 are rejected under 35 U.S.C. 102(a) as being anticipated by Hemphill (October 1996).

Hemphill discloses the instantly claimed invention directed to a culture of cells that exhibits attenuation relative to the parent strain, wherein the culture of cells comprises monkey kidney cells infected with a *Neospora* strain that is temperature sensitive culture of cells that

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comprises NC-1 Neospora in Vero cells, wherein Vero cells are monkey kidney cells. The cells were maintained in culture and passaged at least once a week (see Material and Methods, page 4279, col. 2). The cells were used to produce a composition of cultured cells together with a pharmaceutically acceptable carrier, phosphate buffered saline (see top of page 4280, col. 1, paragraph 1).

The compositions of cultured NC-1 Neospora cells in Monkey kidney cells would be attenuated through the one or more in-vitro passages used to maintain the tachyzoites (definition provided in Instant Specification, page 5, lines 17-27). By all comparable data, the disclosed culture of cells of NC-1 is the same or equivalent culture of cells now claimed. The cells would be sensitive to freezing temperature. Inherently, Hemphill discloses and anticipates the now claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594

13. Claims 1-2, 6-7, 13-14 and 17-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Kim et al (US Pat. 5,976,553).

(Instant claims 1-2, 6-7) Kim et al disclose and claim an attenuated strain of Neospora (see claim 4) that has been attenuated through transformation with a specific DNA sequence (see col. 16, lines 16-18; col. 15, lines 38-50; col.16, lines 37-40) and are combined with cytomix buffer (see col. 16, lines 8-9).. The strains would be sensitive to freezing temperatures.

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(Instant claim 13-14, 17-18) The claimed cultured strains of Neospora were disclosed to be prepared by a repeatable method for Neospora derived strains that comprises the steps of:

Modifying cells from a pathogenic parent strain of a species of Neospora (see col. 7, lines 44-52, especially line 52; col. 15, lines 37-67 and col. 17, lines 1-44; stable transfection; see claim 4, col. 10, lines 65-67);

Selecting and clonally propagating one or more modified cells (see col. 11, lines 19-29; col. 11, lines 46-50);

Selecting and clonally propagating one or more attenuated cells which are capable of triggering an immune response (see col. 11, lines 60-63) and combined with a veterinarily acceptable carrier ("cytomix buffer; see col. 16, lines 8-9, parasite cells that have been treated with cytomix buffer).

Inherently, the attenuated strain of Neospora, and method of preparing the strain(s) are disclosed by Kim et al anticipate the now claimed invention.

Double Patenting

14. Claim 1-4 and 6-9 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,656,479. Although the conflicting claims are not identical, they are not patentably distinct from each other because The instant claims are directed to a genus of attenuated Neospora cells; the allowed species anticipates the instantly claimed genus; the instantly claimed genus is obvious over the allowed species.

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Conclusion

15. This is a non-final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on 8:30-6:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
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LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600